REMARKS

Claims 1, 26, 31, 32, 36 have been amended. Claims 4, 5, 29, and 30 have been cancelled. No new matter has been added. Upon entry of this amendment, claims 1-3 and 7-28, and 31-40 are present and active in the application.

Interview Summary

Applicants would like to thank Examiner Shahrestani and Examiner Casler for their helpful discussion with Applicants' representatives on February 7, 2008. During this discussion, it was agreed that Applicants would clarify the term plasmon resonant in claim 1. Applicants' representative also pointed out that independent claim 22 included elements which are not found in any of the cited references.

Request for Reconsideration

When imaging biological tissues, it is often desirable to enhance the signals measured from specific structures. Contrast agents, which produce a strong emission or reflection signal, have been utilized in virtually every imaging modality including ultrasound, computed tomography, magnetic resonance imaging, and optical microscopy.

Optical coherence tomography (OCT) is an emerging high-resolution medical and biological imaging technology. OCT is analogous to ultrasound B-mode imaging except reflections of low-coherence light are detected rather than sound. OCT detects changes in the backscattered amplitude and phase of light from structures in tissue. This imaging technique is attractive for medical imaging because it permits the imaging of tissue microstructure in situ, yielding micron-scale imaging resolution without the need for excision and histological processing. OCT can record structures such as cell membranes, nuclei, and other organelles based on morphology-dependent optical characteristics. Because OCT performs imaging using light, it has a one- to two-order-of-magnitude higher spatial resolution than ultrasound and does not require contact with tissue.

Despite the rapidly growing acceptance of OCT in biomedical imaging, there are presently few agents available for enhancing optical contrast. This is partly attributable to the use of NIR wavelengths (>800 nm) that are typically employed in OCT, which are outside the range of most optically active materials.

The present invention makes use of the discovery that *anisotropic* metallic nanoparticles can be used to enhance the contrast in analyses and imaging techniques that use electromagnetic radiation, particularly those techniques which use radiation in the frequency range of infrared to ultraviolet, such as optical coherence tomography, light microscopy, holography, confocal microscopy, polarization microscopy, interference microscopy, multi-photon microscopy, and endoscopy. Moreover, metallic nanoparticles composed of gold, silver, and/or copper are particularly suited as contrast agents for OCT applications. A*nisotropic* metallic nanoparticles possess superior plasmon-resonant characteristics and may be fabricated in bimetallic forms to permit their use in OCT applications using switchable magnetic and electric fields. The nanoparticles efficiently absorb the incident optical radiation and can be used as hyperthermia agents, creating local thermal gradients that are sufficient to kill individual cells. These contrast agents can therefore be used simultaneously for the detection and imaging of targeted cells followed by hyperthermic ablation.

Double Patenting

Applicants respectfully request that the provisional rejection of the pending claims under the judicially created doctrine of obviousness-type double patenting over claims 1-25 of U.S. Patent No. 7,198,777 (Boppart et al.) be withdrawn. The present application and Boppart et al. are not commonly owned, and were not developed as part of a joint research agreement.

Applications having different inventive entities can only be rejected on the ground of double patenting when one of two conditions is met: a) the applications are commonly owned, or b) the claimed invention resulted from activities undertaken with the scope of a joint research agreement as defined in 35 U.S.C. § 103(c)(3). See MPEP §§ 804.03(I) and 804.03(II). The present application is jointly owned by the Board of Trustees of University of Illinois and by the Purdue Research Foundation. In

contrast, Boppart et al. is owned solely by the Board of Trustees of University of Illinois. Thus, the applications are not "commonly owned" as defined in MPEP § 706.02(l)(2). In addition, the inventions claimed in the present application and in Boppart et al. were not made by or on behalf of parties to a joint research agreement that was in effect on or before the date the claimed inventions were made. Thus, the applications do not meet the requirements for a rejection based on obviousness-type double patenting.

In addition, a complete *prima facie* case of obviousness-type double patenting over the claims of Boppart et al. has not been presented, since every element of the pending claims is not found in the claims of Boppart et al., nor obvious over the claims of Boppart et al. The only reasoning provided by the Office for applying the double patenting rejection is that

> ... [a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because they represent obvious alternative variations and groupings of the patented claims. (Office Action dated December 31, 2007, page 3)

However, as noted above, independent claim 1 includes the claim element "wherein the mixture comprises the sample and *anisotropic metallic nanoparticles*", which is not present in the claims of Boppart et al. Thus, the claims of Boppart et al. cannot be fully-encompassed by the pending claims. Since all elements in the pending claims have not been considered, a *prima facie* case of obviousness-type double patenting has not been presented. See MPEP § 2143.03. Withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. § 103(a)

The rejection of claims 1-21 under 35 U.S.C. § 103(a) as being unpatentable over Toublan et al. (NPL-"Magentically-inducible optical contrast agents for optical coherence tomography"), is respectfully traversed. Claim 1 of the present invention addresses the problem of forming an image of a sample comprising forming an image of a mixture, by exposing the mixture to electromagnetic radiation. The mixture comprises the sample and *anisotropic metallic nanoparticles* that have an extinction coefficient of at least $10^6\ M^{-1}cm^{-1}$ at a frequency in the range of 10^{12} to 10^{17} Hz. The electromagnetic radiation is in the frequency range of infra-red to ultraviolet light.

Toublan et al. is directed to contrast agents in medical and biological imaging to enhance the sensitivity of detection and improve the diagnostic ability of imaging techniques. Toublan et al. further discusses using *microspheres* of 0.5 to 5 microns in diameter with a 50 Å thick protein shell as optical contrast agents. The microspheres can be filled with scattering substances such as melanin or gold. Scattering substances such as melanin or gold are not necessarily *anisotropic* nanoparticles, since being an *anisotropic* nanoparticle depends on not only the size of the particle, but the particle's *shape* as well. (See Specification, Paragraphs [0031] and [0049])

The Examiner maintains that Toublan et al. teaches material within the microspheres of varying shapes and sizes, and points to FIG. 1 for support of this proposition. (Office Action dated December 31, 2007, page 4) While FIG. 1 of Toublan et al. illustrates microspheres of varying shapes and sizes, it does not teach that the material within the microspheres is *anisotropic* nanoparticles. Toublan et al. does not teach or disclose anywhere that the size or shape of the material within the microspheres conforms to that of an *anisotropic* nanoparticle.

The rejection of claims 22-40 under 35 U.S.C. § 103(a) as being unpatentable over Sokolov (US 2004/0023415) in view of Lee et al. (NPL-"Engineered Microsphere Contrast agents for Optical Coherence Tomography"), is respectfully traversed. Claim 22 of the present invention addresses the problem of forming an image by optical coherence tomography, including exposing a patient to electromagnetic radiation, collecting reflected electromagnetic radiation, and forming an image from the collected electromagnetic radiation. The improvement comprises administering *anisotropic metallic nanoparticles* to a patient to *enhance contrast* of the image, wherein the anisotropic metallic nanoparticles are *gold nanorods* with a *magnetic tip*.

Sokolov discloses methods and apparatuses for using biospecific contrast agents to enhance the imaging of cells. Even more particularly, it concerns using metal nanoparticles and quantum dots attached to probe molecules with a high affinity to a specific biomarker on the surface of pre-cancerous and cancerous cells to enhance the imaging of those cells. Sokolov also discloses that colloidal gold and silver nanoparticles exhibit beautiful and intense colors in the visible spectral region. (See Sokolov, paragraph [0071]). Sokolov then states that it is believed that these colors are

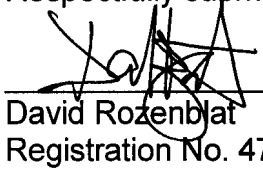
the result of excitation of surface plasmon resonances in the metal particles and are extremely sensitive to particles' sizes, shapes, and aggregation state; dielectric properties of the surrounding medium; adsorption of ions on the surface of the particles; etc. However, Sokolov does not teach or disclose *administering anisotropic* metallic nanoparticles to a patient. In fact, there is no mention whatsoever in Sokolov of using *anisotropic* metallic nanoparticles, and no reason is given as well.

Furthermore, Sokolov fails to teach or disclose *anisotropic* metallic nanoparticles which are gold *nanorods* with a *magnetic tip*. There is no teaching or disclosure within Sokolov of using a nanorod at all, let alone a gold nanorod with a *magnetic tip,* since that would require a tip that is *not gold, and such a tip is not disclosed*. Furthermore, Lee et al. fails to cure all of the deficiencies of Sokolov. As a result, Applicants maintain that claims 22-40 are not anticipated by or obvious in view of the cited references, either alone or in combination.

CONCLUSION

Applicants submit that the application is now in condition for allowance. Early notice of such action is earnestly solicited.

Respectfully submitted,



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